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A RARE CASE REPORT: MUCOPOLY-SACCHARIDOSIS (HURLER SYNDROME) WITH RACHITIC CHANGES IN A NIGERIAN

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ABSTRACT
An unusual presentation of mucopolysacharidosis (Hurler's syndrome), a connective tissue enzyme deficiency disorder with rickets is presented. It was seen in a 3 year old female child. Though facilities to confirm the metabolite in urine were not available, the radiological changes appeared pathognomonic for Hurler Syndrome. They also showed the features of rickets.

ABSTRAIT
Une présentation peu commune de mucopolysachandosis (le syndrome de Hurler), un désordre d'insuffisance d'enzymes de tissu connectif avec le rachitisme est présenté. On l'a vu dans un enfant féminin âgé de 3 ans. Bien que les équipements pour confirmer le métabolite en urine n'aient pas été disponibles, les changements radiologiques ont semblé pathognomonic pour le syndrome de Hurler. Ils ont également montré les dispositifs du rachitisme.

CASE REPORT
A 3 year old female presented in an outpatient paediatric clinic with persistent nasal discharge and progressive abdominal enlargement of 2 years and 8 months duration. Other associated problems included delayed speech development, hearing impairment, knock knees.
At 6 months of age, her parents observed she did not look normal hence they confined her indoors most of the time. None of her other siblings (four) had similar problems.
On examination she had coarse facies with frontal bossing, bilateral corneal clouding and depressed nasal bridge. She had copious nasal discharge.
Her apex beat was at the fifth left intercostal space lateral to the mid clavicular line. Auscultation of the lung fields yielded transmitted sounds. The abdomen was distended with hepatomegaly of 6cm below the costal margin. She also had short sturdy fingers with swelling of both wrists, kyphoscoliosis and bilateral genu valgus.

A clinical diagnosis of Hurlers syndrome was made. Urinary glycosaminoglycans level could not be obtained but alkaline phophatase level was raised 557iu/l. There were classical radiological features both of Hurlers syndrome and rickets. She had vitamin D replacement therapy but absconded from follow up.

A search for this association of Hurlers syndrome with rickets was not easily available in documented literature hence the need to publish it.

Discussion:
The mucopolysaccharidoses form a rare group of abnormalities with prominent recognizable radiological features. Incidence is about 1 in 150,000 infants. These inherited disorders consist of 6 major types as follows: Morquio-Brailsford type (MPS-IV), Hurler-Scheie type (MPS1-H), Maroteaux Lamy disease, spondyloepiphyseal dysplasia, Diatrophic dwarfism, metatrophic dwarfism etc. Morquio and Brailsford described this clinical entity (Morquio-Brailsford) simultaneously and

independently in 1929 in Montevideo, Uruguay and Birmingham, England respectively[1].

Hurler syndrome was first identified by a German paediatrician, Gertrud Hurler (1889 1965) in 1919, Scheie, an ophthalmologist described a mild form of Hurler syndrome called Hurler syndrome type V[2] . Hurler syndrome is one of the commonest forms of mucopolysaccharidoses and is autosomal recessive like most other types of MPS. In Hurler syndrome, there is a deficiency in the enzyme, alpha L-iduronidase. Because the body is unable to metabolize the glycosaminoglycans (commonly referred to as GAGs) there is an excessive accumulation of complex carbohydrates called mucopolysaccharides in connective tissue. GAGs are produced by the body and are present in all types of connective tissue. Connective tissue gives structural support to organs. Almost all organs are involved. This results in progressive damage and ultimately to the numerous clinical, radiological and laboratory changes seen in these individuals. This patient manifested grotesque features of Hurler clinically.

These children appear normal at birth but the characteristic pathological features begin to appear by the age of 6months to 1 year as was the case with this child. The clinical features include coarse, thick, facial features, prominent dark eye-brows, depressed nasal bridge, full lips, thick large tongue, cloudy corneas, progressive stiffness and obvious mental retardation. The heart and heart valves may be involved and such cardiac effects mostly lead to death during teenage age. Our patient did not have this manifestation though there was no echo study. These patients have short stature (especially short trunk). This may occasionally pose some diagnostic difficulty when differentiating Hurler's syndrome from other forms of dwarfism. Hirsutism, shortness of breath, stiff joints, umbilical hernia, claw hand are other clinical features that may be visualized

Clinical examination may reveal a combination of the following: Hepatomegaly, as seen in the present case, splenomegaly, inguinal hernia, flared nostrils, enlarged tongue, retinal pigmentation, hip dislocation, kyphosis, heart murmurs etc.

Laboratory investigations especially urine show increased amounts of dermatan sulphate and heparin sulphate and is the gold standard for diagnosis of Hurler syndrome. These however were not conducted in this child because of non availability of the reagent. Other advanced tests include detecting the absence of lysosomal alpha L iduronidase in cultured fibroblasts. There is abnormal histologic staining of white blood cells called metachromasia. Prenatal testing involves aminocenthesis for enzyme testing and culture of cells obtained from amniotic fluid. TCG is helpful in detecting cardiac abnormalities. 2 Dimensional echocardiography will also show chamber enlargement and valvular lesions.

Radiological Investigations form a very important part of diagnosis in mucopolysaccharidoses as seen in this patients case. The radiographs of the skull, vertebrae, long bones, pelvis, hand and chest are usually quite informative. In Hurler's syndrome, a J-shaped sella is seen in the skull. This results because of the shallow elongated sella with a long anterior recess extending underneath the anterior clinoid processes.

The ribs show typical widening of the ribs end. There is antero-inferior beaking in the vertebral bodies. The central part of the second lumbar vertebral body is hypoplastic and is displaced somewhat posteriorly resulting in a kyphus deformity. The long bones show swelling of their central aspects due to widening of their medullary canal.

Typical Radiological features of mucopolysaccharidoses IH include a

combination of the following features macrocephaly, thickened calvarium, groundglass appearance, wide ribs, short wide clavicles which are poorly modelled. Ovoid hook-shaped vertebral bodies with thoracolumbar kyphus deformity. Odontoid hypoplasia, flaring of iliac wings with basal constriction of the iliac bones. Small irregular femoral capital epiphyses, coxa valga; the long bones are poorly modelled and have thin cortices. Trabecular pattern of the bones are coarse and the phalanges are short and wide. There is characteristic pointing of the proximal ends of the metacarpals. This patients films displayed classical radiological features of hurler as well as healing rickets. The confinement of the patient by her parents' because of her abnormal appearance may well be responsible for the rachitic changes which ensued since she was not exposed to enough sunlight.

In Morquio Syndrome, the vertebral bodies show generalized flattening of the vertebral bodies with central anterior beaking. Hypoplasia is quite common and there is posterior displacement of L1 or L2 culminating in sharp angular kyphosis. The long bones taper but this feature is not as marked as in Hurler's syndrome. There is flaring, fragmentation and flattening of the femoral heads with irregular deformity of the acetabulum. Subluxation of the hip therefore arises. The viscera and central nervous system should be investigated as well. Generally, anterior beaking of the vertebral bodies may well be visualized in Hurler's, Morquios syndrome, cretinism, or dysostosis multiplex group.

Hurler's syndrome and the dysostosis multiplex group share similar features than morquio. However again, laboratory analysis especially urine, leucocytes, and fibroblastic cultures aid more specific diagnosis.

Neurological changes are best demonstrated by magnetic resonance imaging.

The present case report presents a combination of rachitic features and MPS like the sole report by Gudino et al that had MPS, West syndrome and vitamin D dependent rickets. Rickets is a disorder of bone mineralization in which osteoblastic activity and production of bone matrix continue but mineralization of matrix is delayed. Aetilogy of rickets is divided into two categories: The first category there is diminished or in effective production of active vitamin D. This includes reduced oral intake of vitamin D, limited sunlight, liver disease or vitamin D malabsorption. This patient being discussed seems to fall into the first category possibly because of her parents' reaction due to the fact that she was purposely kept indoors and non of her siblings showed rachitic changes at all. The second category is due to renal abnormalities like fanconi syndrome and renal tubular acidosis Treatment includes vitamin D replacement[5].

There is no known definitive treatment for Hurler syndrome. The only attempt at treatment is bone marrow or cord blood transplant. The bone marrow transplant is preferably before the age of 2 years. The patient defaulted to follow up.

Generally however, life expectancy if left totally untreated in MPS I-H is only 5-10 years. The oldest Hurler survivor of a bone marrow transplant is in his early twenties. Enzyme replacement therapy could be attempted and has been approved in the USA and Europe.

A Study in a Cuban population claimed to offer genetic counselling to affected families[5].

X-RAY FINDINGS

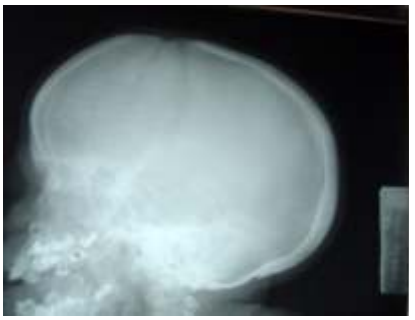

Fig. 1 SKULL

Macrocephaly with ground glass appearance (also seen in Achondroplasia)
Calvarium is thickened.
Sella is widened in anteroposterior direction tending towards a J-shape.
Thinned occiput (relative to the rest of the calvarium).

SPINE

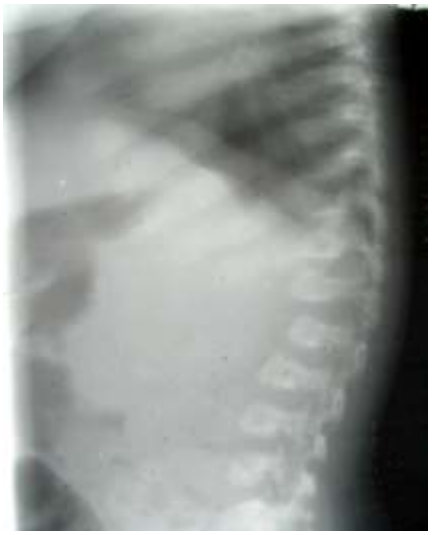

Fig.2

Second lumbar vertebrae is diminished in size. It is slightly displaced posteriorly resulting in kyphosis at the lumbar region.
Antero-inferior beaking of the vertebrae especially lumbar.

HANDS AND FOREARM

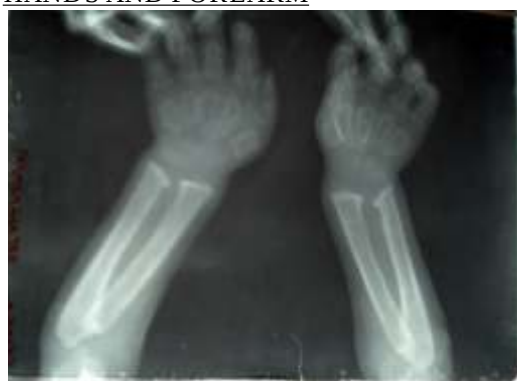

Fig. 3

Widened phalanges.
Pointing of the proximal ends of the metacarpals.
Bevelling of the distal ends of the radius and ulna(both ulna metaphyses)
Dense horizontal band at the distal end of the radius and ulna.
Cupping of the right ulna.
Transverse bands also seen in distal radial shaft (growth arrest lines)
Irregularity of shaft of radius in the medial border.

KNEES (mostly rachitic)

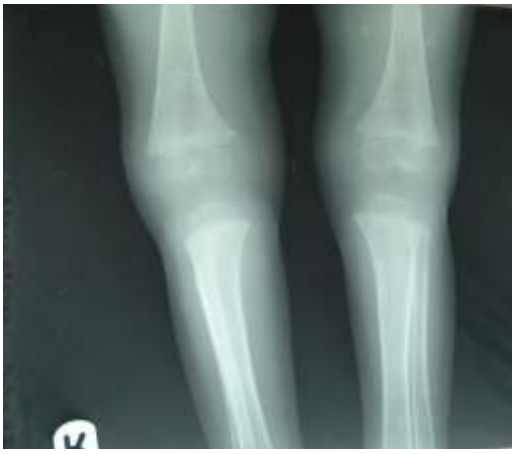

Fig. 4
Distal femora are widened(flared)(a rachitic feature)
Transverse lines in the diaphysio-metaphyseal ends. (growth arrest lines)
Some flaying of the medial part of metaphyses of the tibia.
Growth arrest lines in the tibiae.
Slight anterior bowing of the tibia.

PELVIS (small and square in achondroplasia)
Iliac wings are flared.
Elongated femoral neck.
Acetabular roofs appear shallow(also seen in achondroplasia)
Interpedicular distance is normal unlike in achondroplasia where it progressively narrows down to fifth lumbar.

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